Remarks

I. Summary of the Office Action

In the Office Action dated December 10, 2009, the Examiner has withdrawn the objection to claims 42, 49, 56, and 58 and the rejection of claims 50 and 59 under 35 U.S.C. § 112, second paragraph. The Examiner has maintained rejections under 35 U.S.C. §§ 102 and 103 and on the grounds of nonstatutory obviousness-type double patenting. Applicants respectfully request reconsideration of the outstanding rejections.

II. Detailed Action Section

Under the section entitled Detailed Action, the Examiner has provided the status of the application following Applicants' filing of an Amendment and Reply Under 37 C.F.R. § 1.111 on August 17, 2009 ("Amendment and Reply"), which has been acknowledged. *See* Office Action, page 2. The Examiner notes, however, that "[a] search was conducted on the elected species, SEQ ID NO: 3, and a prior art was found." *Id.* Yet, the Office Action does not appear to apply any alleged prior art that has not already been applied in the previous non-final Office Action, mailed January 30, 2009. Applicants respectfully request that if indeed any alleged prior art was identified in the Examiner's search, that finality be withdrawn and that such alleged prior art be made of record, and applied if applicable, so as to avoid any additional burden and cost in the prosecution of this application. *See, e.g.*, M.P.E.P. §§ 707.07(g) and 904.03.

III. Summary of Applicant's Reply

Applicants respectfully assert that the outstanding rejections under 35 U.S.C. §§ 102 and 103 and for obviousness-type double patenting suffer from misinterpretations of both the claimed subject matter and the applicable law. In brief, Applicants claim new and nonobvious methods of using soluble Nogo receptor-1 (NgR1) polypeptides based on the discovery and elucidation of the involvement of NgR1 in Aβ peptide processing and deposition into plaques. This interaction could not have been predicted based on the studies of the Nogo ligand-NgR1 signaling pathway, which controls neurite outgrowth and neuroplasticity, as described in Lee *et al.* (U.S. Pub. No. 2005/0271655; "Lee") and Strittmatter (U.S. Pub. No. 2002/0077295; "Strittmatter"). These studies have shown that a soluble NgR1 polypeptide could reverse the Nogo-mediated inhibition of neurite outgrowth in, *e.g.*, neuronal diseases or injuries where the neurons are damaged either by physical trauma or disease pathogenesis such as plaque deposition, by, *inter alia*, forming new axonal connections. However, such studies do not make it known or obvious to a person of ordinary skill in the art that a soluble NgR1 polypeptide could be used in an entirely unrelated pathway to reverse and treat the underlying disease pathogenesis—which is what the claimed methods do.

The rejections of the present method claims, whether for alleged lack of novelty or obviousness, are grounded in one recurrent and misapplied theme, inherency. To support this inherency theme, the rejections ignore claim language and lack any factual or technical reasoning as to why the prior uses of soluble NgR1 polypeptides to promote axonal outgrowth anticipate or render obvious the claimed methods of reducing Aβ peptide and plaque deposition. To demonstrate inherency requires that the missing

descriptive matter must necessarily be present in the prior art reference, not merely probably or possibly. This standard has not been met, and the prior art does not preclude the claimed new uses of soluble NgR1 polypeptides.

III. The Rejections over Lee and Strittmatter Under 35 U.S.C. § 102(e) and (a) are Traversed

At pages 3-7 of the Office Action, the rejection of claims 42, 44-47, 49-50, 52-56, 58, and 59 under 35 U.S.C. § 102(e) and (a) as allegedly being anticipated by Lee has been maintained. At pages 7-11 of the Office Action, the rejection of claims 42, 44-47, 50-56, 59, and 60 under 35 U.S.C. § 102(e) and (a) as allegedly being anticipated by Strittmatter has also been maintained. Applicants respectfully disagree and request that the maintained rejections be reconsidered in view of the following remarks.

A. Summary of Claimed Subject Matter and Applicants' Invention

Applicants claim methods of treating a disease, disorder, or condition by reducing the levels of Aβ peptide in a mammalian brain and of treating a disease, disorder or condition associated with plaques of Aβ peptide in a mammalian brain. *See* claims 42 and 52. The methods comprise administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits, wherein the soluble Nogo receptor-1 polypeptide comprises an NT domain, eight leucine-rich repeats, and an LRRCT domain. The claimed methods are based on Applicants' discovery and elucidation of the involvement of NgR1 in Aβ peptide processing and deposition into plaques. *See* specification, ¶ [0004]. This point is important to understanding how the present invention is different from the prior art methods of Lee and Strittmatter, which

focus on the Nogo ligand-NgR1 signaling pathway and its role in neurite outgrowth and neuroplasticity.

For example, the present invention is based on the discovery that NgR1 interacts with amyloid precursor protein (APP) and binds its Aβ region, as well as to the processed Aβ peptide. *See id.* at Example 2, ¶¶ [0060]-[0064]. Applicants demonstrated that the interaction between NgR1 and Aβ peptide occurs at a distinct site on NgR1 from the interaction with the known NgR1 myelin ligands Nogo, OMgp, and MAG. *See id.* at Example 3, ¶ [0065]. Applicants showed that as a result of the interaction of NgR1 with APP, Aβ peptide production was enhanced and NgR1-Aβ peptide binding was increased. *See id.* at Examples 4 and 5, ¶¶ [0066]-[0068]. Based on these studies, Applicants then demonstrated that the administration of a soluble NgR1 polypeptide to mice that are predisposed to over-production of Aβ peptide and increased deposition of Aβ peptide into amyloid plaques, not only reduced the levels of Aβ peptide, but also reduced its deposition into amyloid plaques. *See id.* at Example 6, ¶¶ [0069]-[0070]. Thus, Applicants demonstrated that NgR1 interacts in an entirely new pathway that is distinct from the NgR1-Nogo ligand pathway and that a soluble NgR1 polypeptide could be used to reduce the levels of Aβ peptide and its deposition into amyloid plaques.

B. The Methods of Lee and Strittmatter Do Not Inherently Anticipate the Claimed Subject Matter

The Examiner alleges that the methods of Lee and Strittmatter inherently anticipate the claimed methods because the same "active method step" is allegedly disclosed. *See* Office Action, pages 7 and 11. This simply is not the case.

Lee and Strittmatter do not anticipate the claimed methods because neither reference discloses or suggests methods comprising administering a soluble NgR1

polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits. Anticipation requires that all the elements and limitations of the claims are found, either explicitly or inherently, within a single reference, arranged in the same way as the claim. *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1370 (Fed. Cir. 2008). The absence of any claimed element from the reference negates anticipation. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1574* (Fed. Cir. 1984). Lee teaches, *inter alia*, "a method of promoting survival of a neuron at risk of dying, comprising contacting the neuron with an effective amount of . . . a soluble NgR1 polypeptide." Lee, ¶ [0021]. Strittmatter teaches, *inter alia*, "a method of treating a central nervous system disease, disorder or injury, e.g., spinal cord injury" comprising administering an effective amount of a soluble NgR1 polypeptide." Strittmatter, ¶ [0022]. Contacting a neuron with or administering a soluble NgR1 polypeptide is not the same as administering a soluble NgR1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits. Thus, this "active method step," as characterized by the Examiner, is absent in the teachings of Lee and Strittmatter.

Furthermore, the missing descriptive matter is not necessarily present in Lee and Strittmatter. When a reference does not explicitly teach all elements of a claim, anticipation can be shown by inherency if, and only if, the cited reference makes clear that the missing descriptive matter is necessarily present in the thing described in the reference. *Continental Can Co. USA Inc. v. Monsanto Co.*, 948 F.2d 1264 (Fed. Cir. 1991). Inherency may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. *In re*

Robertson, 169 F.3d 743, 745 (Fed. Cir. 1999). Lee and Strittmatter are directed to, *inter alia*, the use of soluble NgR1 antagonists in the NgR1-Nogo ligand signaling pathway, which controls neurite outgrowth and neuroplasticity. Thus, the result of using the NgR1 antagonists in the methods of Lee and Strittmatter is to reverse the Nogo-mediated inhibition of neurite outgrowth in, *e.g.*, neuronal diseases or injuries where the neurons are damaged either from physical trauma or disease pathogenesis such as plaque deposition, by forming new axonal connections. Lee and Strittmatter, however, are silent as to the interaction of soluble NgR1 polypeptides with APP or Aβ peptide, and on reducing levels of Aβ peptide or of plaque deposits as claimed in the presently claimed methods. That such methods are *necessarily* present in Lee and Strittmatter has not been demonstrated.

Applicants respectfully assert that the Examiner has not satisfied her burden of establishing that the alleged missing descriptive matter of Lee or Strittmatter, administering a soluble NgR1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits, is necessarily present.[1] Other than a mistaken assertion that Lee and Strittmatter disclose the same "active method step" as presently claimed, the Examiner has provided absolutely no basis in fact and/or technical reasoning in support of the determination that the alleged missing descriptive matter necessarily flows from the teachings of Lee or Strittmatter. *Id.* While

[1] During the prosecution of a patent application before the Office, the burden of establishing that the inherent characteristic necessarily and invariably functions in accordance with the limitations of the claim is on the Examiner. M.P.E.P. § 2112. And, in order to satisfy the Examiner's burden, the rejection based on inherency must be accompanied by factual evidence and/or technical reasoning. *See Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) ("In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." (emphasis in original)).

it is *possible* that administering a soluble NgR1 polypeptide according to the prior art methods might result in the reduction of Aβ peptide should Aβ peptide happen to be present, this possibility simply has not been shown to *necessarily and invariably* occur. Until Applicants' discoveries, NgR1 had not been implicated in the entirely novel and nonobvious pathway of Aβ peptide processing and deposition into plaques.[2]

Furthermore, the principles of inherency do not preclude the new use of soluble NgR1 polypeptides to treat patients in need of reduced levels of Aβ peptide or plaque deposits, because "[n]ew uses of old products or processes are indeed patentable subject matter." *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1378 (Fed. Cir. 2005). In *Perricone*, the Federal Circuit held that the claimed method of treating skin sunburn by topically applying a fatty acid ester of ascorbic acid was not inherently anticipated by a prior art reference that disclosed the topical application of a fatty acid ester of ascorbic acid to the skin. *Id.* at 1379. The court noted that the reference did not disclose topical application to skin sunburn and was silent as to "any sunburn prevention or treatment benefits, not to mention the mechanisms underlying such uses." *Id.*

The Federal Circuit's analysis in *Perricone* is directly on point with the present method claims. For example, whereas Lee discloses the administration of soluble NgR1 polypeptides to a mammal displaying signs or symptoms of a genus of diseases and injuries that includes Alzheimer's disease, Lee does not disclose, and is silent as to,

[2] For example, Strittmatter, S.M., J. Mol. Neurosci. 19:117-121 (2002) ("Strittmatter 2002"; cited in Office Actions mailed January 30, 2009, and August 6, 2008), suggested the use of Nogo-NgR1 inhibitors to promote increased axonal growth as a means to recover lost synaptic connections in cells affected by neuronal loss from Aβ peptide plaque deposits. Strittmatter 2002, page 117, first column. However, Strittmatter 2002 indicated that such therapy would be useful only "if successful therapies are developed to delay or halt neuronal death in [Alzheimer's disease]." *Id.* It is this latter therapy to delay or halt neuronal death to which the present methods are directed, through the reduction of Aβ peptide and plaque deposits, that the Examiner has failed to establish that Lee or Strittmatter necessarily discloses.

administration of soluble NgR1 polypeptides to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits. Strittmatter is even further afield from Lee because Strittmatter discloses administration of soluble NgR1 polypeptides to treat a CNS disease, disorder, or injury and not Alzheimer's disease in particular. Moreover, neither Lee nor Strittmatter mentions the mechanism underlying the reduction of levels of Aβ peptide and plaque deposits, which is mediated through the interaction of NgR1 with APP and Aβ peptide and is entirely different from the Nogo-NgR1 mechanism described in Lee and Strittmatter. The mechanism of the present invention would not necessarily and invariably occur under the methods described by Lee or Strittmatter.

Thus, based on a very similar factual scenario to the present claims and asserted art, the Federal Circuit in *Perricone* held that the claimed method of treating skin sunburn by topically applying a fatty acid ester of ascorbic acid was not inherently anticipated by the prior art disclosure of topically applying the same composition. Applicants respectfully assert that the present methods of claims 42 and 52 are not inherently anticipated by Lee or Strittmatter, at least because the Federal Circuit's ruling in *Perricone* dictates otherwise.

C. The Genus of Methods of Use Described in Lee and Strittmatter Do Not Inherently Anticipate the Claimed Subject Matter

The Examiner also alleges that the genus of diseases, disorders, and injuries disclosed in Lee and Strittmatter as treated by soluble NgR1 polypeptides is such that "one of ordinary skill in the art would at once envisage the administration of an Alzheimer's patient with the Nogo receptor-1 polypeptide." Office Action at pages 6 and

11. This genus-species analogy, however, fails to appreciate the fact that the claimed methods are not species that are envisionable within the genera of Lee and Strittmatter.

The standard for anticipation of a species by a genus is that a person of ordinary skill in the art must be able to immediately envisage a particular species element for that species to be enabled. *See, e.g.*, *In re Petering*, 301 F.2d 676, 681 (C.C.P.A. 1962) (distinguishing a broad genus of chemical compounds (species not enabled) from a subgenus of approximately 20 readily-envisionable species (each species therein enabled)). If the members cannot be envisioned, the reference does not disclose the species and the reference is not enabling with respect to that species. *Impax Laboratories, Inc. v. Aventis Pharmaceuticals, Inc.* 468 F.3d 1366, 1383 (Fed. Cir. 2006).

As discussed above, the methods of Lee and Strittmatter are directed to an entirely different mechanism than presently claimed for methods of using soluble NgR1 polypeptides. The alleged "genus" of Lee and of Strittmatter comprises treating conditions wherein the soluble NgR1 polypeptide acts to disrupt the Nogo ligand-receptor signaling pathway, which mediates, *e.g.*, neurite outgrowth and axonal regeneration, for various diseases, disorders, and injuries, including Alzheimer's disease as disclosed in Lee. By contrast, the presently claimed methods of reducing levels of Aβ peptide or plaque deposits is not a species within either alleged genus of Lee or Strittmatter because, *inter alia*, the soluble NgR1 polypeptide is acting to disrupt interaction with APP, Aβ peptide processing, and plaque formation. Therefore, a person of ordinary skill in the art looking at Lee or Strittmatter would not possibly envisage that

administering a soluble NgR1 polypeptide would reduce the levels of Aβ peptide or plaque deposits as alleged.

Furthermore, even if the genus of Lee or of Strittmatter was broad enough to encompass methods of reducing levels of Aβ peptide or plaque deposits, based solely on the prior administration of a soluble NgR1 polypeptide, neither genus "inherently disclose[s] all species within that broad category." *Metabolite Labs., Inc. v. Laboratory Corp. of America Holdings*, 370 F.3d 1354, 1367 (Fed. Cir. 2004) (citing *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1262 (Fed. Cir. 1989) ("Under [defendant's] theory, a claim to a genus would inherently disclose all species. We find [this] argument wholly meritless . . . ."). The prior administration of a soluble NgR1 polypeptide, even in Alzheimer's disease, would do nothing more than suggest investigation into further uses of the soluble NgR1 polypeptide to reverse the Nogo-mediated inhibition of neurite outgrowth by forming *new* axonal connections, not into the subject matter of the claimed methods. And, as stated by the Federal Circuit in *Metabolite*, "[a]n invitation to investigate is not an inherent disclosure."[3] 370 F.3d at 1367.

D. Conclusion

In summary, no portions of Lee or Strittmatter, either expressly or inherently, teach the interaction of NgR1 with APP and Aβ peptide or methods comprising administering a soluble NgR1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits. Further, Applicants

[3] In *Metabolite*, the prior art reference disclosed "a broad genus of potential applications of its discoveries." 370 F.3d at 1367. However, rather than the prior art necessarily containing the claimed correlating step of the claimed method, the court stated that the reference "simply invites further

respectfully assert that the Examiner has not met her burden of establishing that the disclosure of Lee or Strittmatter anticipates, either expressly or inherently, each and every element of the methods of claims 42 and 52, and the claims dependent thereon. Accordingly, Applicants request reconsideration and withdrawal of these maintained rejections.

V. The Rejection over Lee Under 35 U.S.C. § 103(a) is Traversed

At pages 11-18 of the Office Action, the rejection of claims 42, 44-47, 49-56, and 58-60 under 35 U.S.C. § 103(a) as allegedly being obvious over Lee has been maintained. *See* Office Action, page 12. Applicants respectfully disagree.

Applicants assert that the Examiner has yet to meet the burden of establishing a *prima facie* case of obviousness based on the applicable law and the guidance provided in the MPEP for formulating obviousness rejections. *See* MPEP § 2143. Specifically, the Examiner has not established on the record that the ordinary artisan reading Lee would *predictably* arrive at claims 42 and 52, which are drawn to methods of treating a disease, disorder, or condition comprising administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits. As discussed above, Lee does not expressly or inherently disclose the administration of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits.

The Examiner maintains to the contrary that the claimed methods are obvious in view of Lee. In particular, the Examiner recycles very similar arguments as applied for

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experimentation to find such [correlations]." *Id.* Such "[a]n invitation to investigate is not an inherent disclosure." *Id.*

Lee under 35 U.S.C. § 102(e) and (a) discussed above, which are based on inherency. *See id.* at pages 15-18. Applicants respectfully point out to the Examiner, however, that "[o]bviousness cannot be predicated on what is *not known* at the time an invention is made, even if the inherency of a certain feature is later established." MPEP § 2141.02 (emphasis added); s*ee also In re Spormann*, 363 F.2d 444, 448 (C.C.P.A. 1966); *In re Rijckaert*, 9 F.3d 1531 (Fed. Cir. 1993). As discussed at length above, at the time of the present invention, it was *not known* that NgR1 interacts in an entirely new pathway that is distinct from the NgR1-Nogo ligand pathway described in Lee and that a soluble NgR1 polypeptide could be used to reduce the levels of Aβ peptide and its deposition into amyloid plaques. As indicated in the present specification, Applicants were the first to elucidate and characterize this relationship. *See, e.g.*, the specification at Examples 1-6, ¶¶ [0058]-[0070]. Therefore, because Applicants' claims are directed to subject matter that was not known at the time the present invention was made, any obviousness argument grounded in the alleged inherent teachings of Lee must fail.

Furthermore, the obviousness inquiry requires that in determining the differences between the prior art and the claims at issue, the claimed invention as a whole, not the differences themselves, must be considered. *See* MPEP § 2141.02; *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530 (Fed. Cir. 1983). The maintained argument that Lee renders the present method claims obvious runs afoul of this requirement. In particular, the allegations that Lee "explicitly teaches the same active method steps of instant claims," or that Lee "teaches the same patient population," is simply not true. *Id.* at page 13 and 16. Applicants respectfully assert that Lee does not teach administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide *to a patient in*

need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits. By reading out at least these differences between the prior art and the claims at issue, the Examiner fails to consider the claimed methods as a whole.

When considering the differences with Lee, the claimed methods as a whole would not have been obvious. As discussed above, Lee teaches, *inter alia*, "a method of promoting survival of a neuron at risk of dying, comprising contacting the neuron with an effective amount of . . . a soluble NgR1 polypeptide" and that the neuron can be in a mammal displaying signs or symptoms of a genus of diseases or injuries that include Alzheimer's disease. Lee, ¶ [0021]. The present method claims are drawn to treating a disease, disorder, or condition by reducing the levels of Aβ peptide in a mammalian brain or treating a disease, disorder or condition associated with plaques of Aβ peptide in a mammalian brain, comprising administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits, respectively. Nowhere does Lee teach these same methods, including the same "active method steps" or that the patient population is those in need of reduced levels of Aβ peptide or in need of reduction of plaque deposits, as alleged by the Examiner.

Furthermore, the person of ordinary skill in the art would not have predictably arrived at the claimed invention as a whole because the methods of Lee treat the disclosed diseases and injuries through an entirely different mechanism than presently claimed for treating a patient in need of reduced levels of Aβ peptide or in need of reduction of plaque deposits. Lee's methods treat diseases and injuries by, *inter alia*, inhibiting the Nogo-mediated inhibition of neurite outgrowth and allowing new axonal

connections to form. Lee, ¶ [0010]. The present methods, however, reduce the levels of Aβ peptide or of plaque deposits through the Nogo receptor-Aβ peptide and/or Nogo receptor-APP interaction, and thus, treat diseases, disorders, or injuries associated with Aβ peptide and plaques thereof. One of ordinary skill in the art reading Lee would not have appreciated that Nogo receptor and Aβ peptide or APP even interact prior to the time the present invention was made. *See, e.g.*, the specification at Examples 1-6, ¶¶ [0058]-[0070]. Therefore, the ordinary artisan reading Lee could not have predictably arrived at the present method claims because there was simply no way of predicting the involvement of NgR1 in an entirely unrelated pathway to reverse and treat the underlying disease pathogenesis associated with Aβ peptide and amyloid plaques.

Accordingly, because Lee does not teach the presently claimed methods as a whole, which comprise administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits, Lee does not make obvious the subject matter of claims 42, 44-47, 49-56, and 58-60. Furthermore, any obviousness argument grounded in the alleged inherent teachings of Lee must fail because Applicants claims are directed to subject matter that was not known at the time the present invention was made. Thus, Applicants respectfully request that the Examiner reconsider and withdrawal the rejection over Lee.

VI. The Rejection on the Ground of Nonstatutory Obviousness-Type Double Patenting is Traversed

At pages 18-20 of the Office Action, the rejection of claims 42, 44, 47, 49-50, 52-53, 56, 58, and 59 on the ground of nonstatutory obviousness-type double patenting over

claims 1 and 7-9 of U.S. Patent No. 7,465,705 ("the '705 patent") has been maintained. *See* Office Action, page 18. The Examiner has again asserted that practicing claims 7-9 of the '705 patent, one of ordinary skill in the art would necessarily achieve the claimed invention and vice versa, because the patient population is not defined. *Id.* at page 19. In addition, the Examiner newly asserts that because "the claims of '705 patent teach[] the same active method steps of instant claims[,]" administering the soluble NgR1 polypeptide in the method claims of the '705 patent would allegedly "inherently reduce the levels of Aβ peptide in a mammalian brain or reduce the plaque deposits in the mammalian brain." *Id.* at page 20. Applicants respectfully disagree and traverse this rejection as it applies to the claims.

Nonstatutory obviousness-type double patenting is analogous to a failure to meet the nonobviousness requirement of 35 U.S.C. § 103 except that the patent underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 600 n.4 (C.C.P.A. 1967). An obviousness-type double patenting analysis generally parallels the guidelines for analysis of a 35 U.S.C. § 103 obviousness determination. *See In re Braat*, 937 F.2d 589 (Fed. Cir. 1991); *see also In re Longi*, 759 F.2d at 895-96; MPEP § 804. Since the analysis employed in an obviousness-type double patenting determination generally parallels the guidelines for a section 103(a) rejection, the factual inquiries that are applied in determining obviousness under section 103 are similarly applied. S*ee Graham v. John Deere*, 383 U.S. 1, 17 (1966).

Applicants respectfully assert that none of the claims of the '705 patent render obvious the claimed invention. Specifically, the methods of claims 7-9 of the '705 patent are directed to inhibiting growth cone collapse of a neuron, decreasing the inhibition of

neurite outgrowth or neurite sprouting in a neuron, and promoting survival of a neuron at risk of dying. In contrast, the present method claims, considered as a whole, are drawn to treating a disease, disorder, or condition by reducing the levels of Aβ peptide in a mammalian brain or treating a disease, disorder or condition associated with plaques of Aβ peptide in a mammalian brain, comprising administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits, respectively. The methods of claims 7-9 of the '705 patent do not teach these same methods, including the same "active method steps" or that the patient population is those in need of reduced levels of Aβ peptide or in need of reduction of plaque deposits, as alleged by the Examiner.

For the same reasons as discussed above for Lee, by reading out at least these differences between the prior art and the claims at issue, the Examiner fails to consider the claimed methods as a whole, as required in the obviousness inquiry. *See* MPEP § 2141.02; *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530 (Fed. Cir. 1983). Furthermore, as also discussed above, because Applicants claims are directed to subject matter that was not known at the time the present invention was made, any obviousness argument grounded in the alleged inherent teachings of the methods of claims 7-9 of the '705 patent must fail.

Therefore, it would not have been obvious from the methods of claims 7-9 of the '705 patent to administer a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide to a patient in need of reduced levels of Aβ peptide or to a patient in need of reduction of plaque deposits. Reconsideration and withdrawal of the rejection

of claims 42, 44, 47, 49-50, 52-53, 56, 58, and 59 on the ground of nonstatutory obviousness-type double patenting over claims 1 and 7-9 of the '705 patent are therefore respectfully requested.

VII. Request for Interview

Applicants have submitted a PTOL-413A form to request an interview before the issuance of a first Office Action on the merits after the filing of a Request for Continued Examination. As required in the interview request form, Applicants have indicated a time and date for the interview. If this time is not convenient for the Examiner, the Examiner is requested to contact the undersigned attorney and reschedule the interview for a mutually convenient time.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Elizabeth J. Haanes, Ph.D.
Attorney for Applicants
Registration No. 42,613

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1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600
1109962_2.DOC